

NOW USP 6,627,571

March 1, 2000 by Lugmair *et al.*, each of which is incorporated by reference for all purposes. The combinatorial library embodied in the array of candidate materials is preferably designed with the assistance of library design software such as LIBRARY STUDIO™ software (Symyx Technologies, Inc., Santa Clara, CA). Preparation of the arrays can be advantageously effected using automated liquid handling robots (e.g., CAVRO Scientific Instruments, Inc.), under control of software such as IMPRESSIONIST™ software (Symyx Technologies, Inc.).

The amount of an individual candidate material deposited as a film (or otherwise included) on a particular portion of the array is not limiting to the invention. The required amount will vary depending upon the required surface area of the film and the required thickness of the film, each of which will, in turn, vary depending upon the chemical process of interest, the geometry of the microreactor, and the required residence time or contact time of reactants in the microreactor, among other factors. In general, the amount of an individual candidate material is typically not more than about 25 mg, preferably not more than about 10 mg, and can be not more than about 7 mg, not more than about 5 mg, not more than about 3 mg and not more than about 1 mg. In preferred embodiments, the amount of an individual candidate material can range from about 0.1 µg to about 100 mg, preferably from about 1 µg to about 10 mg, more preferably from about 10 µg to about 10 mg and most preferably from about 100 µg to about 1 mg.

While an array of one or more films is advantageously employed in connection with the present invention, other array configurations can also be employed to supply the two or more solid-phase candidate materials to a plurality of microreactors. The array can comprise, for example, the candidate materials loaded into the microreactors in bulk form, or as bonded to or linked to porous materials or to microparticles. With reference again to Figure 3, the array can comprise, for example, a substrate 110 having a plurality of wells 130 formed in an exposed surface 112 of the substrate (e.g., Fig. 3E, Fig. 3G) or having a plurality of apertures 140 extending between first and second substantially parallel surfaces 111, 112 of the substrate 110 (e.g., Fig. 3F, Fig. 3H). Such a well 130 or an aperture 140 can comprise a porous material 122 (e.g., Fig. 3E, Fig. 3F) to which a particular candidate material is bonded, preferably covalently bonded. Exemplary porous materials include quartz, glass or alumina, etched microchannels or glass plates, diatomaceous earth, etc. As another alternative, a well 130 or an aperture 140 can comprise microparticles 124, typically referred to in the art as "latex particles" or "beads", to which a particular candidate material is bonded, and preferably covalently

sputtering, ion plating), chemical vapor deposition, plasma-assisted chemical vapor deposition, electrodeposition, electrochemical deposition, coating techniques (e.g., spray drying, spray coating, pyrolysis), and solution-based techniques (e.g., sol-gel, impregnation, precipitation), among others. The film can also be formed by *in situ* growth at a substrate surface, by diffusion of the material into a substrate surface, or by conversion of the substrate material (e.g., thermal oxidation). Such approaches and others are discussed in detail in Bunshah, Handbook of Deposition Technologies for Films and Coatings, 2<sup>nd</sup> Ed., Noyes Publications (1994), and references cited therein. The candidate materials may be applied in discrete, individually addressable regions using mechanical or chemical masking approaches. For example, mechanical masks or shutters can be used in connection with many of the aforementioned deposition techniques to create an array of films in a desired arrangement. Distinct regions of candidate materials may also be formed using film-formation approaches that are or can be controlled to be region-selective – without masking. Spray drying and electrochemical deposition approaches are exemplary region-selective approaches. Different candidate materials may alternatively be applied contiguous to each other. The array can comprise, for example, a contiguous composition gradient of two or more components. Contiguous natural composition gradients can be formed, for example, by multiple-target vapor deposition approaches. See, e.g., Hanak et al., Optimization Studies of Materials in Hydrogenated Amorphous Silicon Solar Cells, Photovoltaic Solar Energy Conference, Berlin (1979), and van Dover et al., Discovery of a Useful Thin-Film Dielectric Using a Composition-Spread Approach, Nature, Vol. 392, No. 12, pp. 162-164 (1998). Contiguous controlled gradients can be formed, for example, by orchestrated (e.g., programmed) masking or shuttering approaches with multi-target deposition, such as those disclosed in copending U.S. patent application Serial No. 09/237,502 filed January 26, 1999 by Wang et al.

Preferred approaches for forming an array of candidate materials include vapor deposition techniques disclosed in U.S. Patent No. 5,776,359 to Schultz et al., sol-gel solution-based techniques disclosed in commonly-owned co-pending U.S. patent application Serial No. 09/156,827, filed January 18, 1998 by Giaquinta et al., electrochemical deposition techniques disclosed in commonly-owned co-pending U.S. patent application Serial No. 09/119,187, filed July 20, 1998 by Warren et al., and *in situ* impregnation techniques for creating arrays of supported catalysts as disclosed in commonly-owned co-pending U.S. patent application Serial No. 09/516,569, filed

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